(54) **Title:** OPTICAL, NONINVASIVE, IN-VIVO MEASUREMENT OF PROPERTIES OF A CONSTITUENT OF A HUMAN OR ANIMAL BODY

(57) **Abstract**

Light of different wavelengths is introduced into a part of the body of a human or an animal, pulsatile fluctuations in the intensity of the light which has propagated through the body are measured. Intensities of light which has propagated through the body and leaves the body at different distance ranges from an entry area are measured for each of at least two wavelengths. From the light intensities estimates of properties of tissue and/or blood are calculated taking into account optical properties of the tissue and the blood influencing the intensities of light leaving the body. The method can for example be applied in pulse oximetry. A device, a probe (2) and a driver/processor (1) for use in the method according to the invention are also described.

TITLE: Optical, noninvasive, in-vivo measurement of properties of a constituent of a human or animal body

FIELD OF THE INVENTION

The invention relates to an optical method for noninvasive, in-vivo monitoring a property of a constituent,
5 such as blood or tissue, of a human or animal body. The invention also relates to a device, a probe and a driver/processor for carrying out that method.

BACKGROUND OF THE INVENTION
10

An example of a measuring method as identified above is pulse oximetry. In clinical practice, this method has become generally accepted for determining the arterial oxygen saturation (S_aO_2).
15   In pulse oximetry, the ratio of relative intensity fluctuations of light of different wavelengths which has passed through a portion of the body is used as an indicator for the S_aO_2. The observed fluctuations are caused by pulsatile changes of the amount of arterial blood in the tissue into
20 which the light has been emitted. The principle underlying pulse oximetry is that the ratio of the relative intensity fluctuations at different wavelengths or wavelength ranges (generally red and infrared and therefore denoted as R/IR) is a function of the ratio of absorption coefficients of arterial
25 blood for these wavelengths or wavelength ranges, which in turn depends on the S_aO_2. By measuring the ratio between the relative intensity fluctuations of the different wavelengths or wavelength ranges, the influence of the magnitude of the pulsations of the amount of arterial blood present in the
30 tissue is believed to be eliminated. Empirically obtained calibration curves are used to calculate S_aO_2 estimates from the measured ratios between the relative intensity

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fluctuations. In this way the influence of light scattering on
R/IR is only partially taken into account.

    Pulse oximetry is usually carried out by transmitting
light through a relatively thin portion of the body, for
5 example through an ear-lobe, a finger, a toe or a part of the
nose.

    A disadvantage of this method is that it cannot be used
if suitable portions of the body cannot be reached. This
problem occurs for example when it is desired to monitor the
10 S_aO_2 of a fetus during labour. Also when the patient suffers
from circulatory problems or when artefacts are caused by
motion of parts of the body available for attachment of the
probe, the use of transmission pulse oximetry is impaired. In
particular in such situations reflectance pulse oximetry is a
15 more appropriate technique for monitoring the S_aO_2. In this
technique, the intensity of light emerging from a part of the
body is measured adjacent to the area where the light has been
introduced into that part of the body instead of in a position
diametrically opposite to the entry area. A probe for carrying
20 out this method comprises an emitter and a detector facing
into essentially the same direction. Such a probe can for
example be held against the fetal scalp during labour or to
any other accessible and free part of the body, provided that
pulsations of sufficient magnitude can be detected at that
25 location.

    From a publication entitled 'Design and Evaluation of an
Instrument to Measure Microcirculatory Blood Flow and Oxygen
Saturation Simultaneously' by Dougherty and Lowry, Journal of
Medical Engineering & Technology, Vol. 16, No. 3 1992, p. 123-
30 128, a method for noninvasively, in-vivo monitoring a property
of a constituent of a human or animal body is known in which
light of at least two, mutually different wavelengths or
wavelength ranges is introduced through an entry area into the
body. Intensities of light of each of the wavelengths or
35 wavelength ranges leaving the body are measured in a first
distance range from the entry area where the light has been

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introduced into the body. Furthermore, an intensity of light
of a wavelength or wavelength range leaving the body in a
second distance range from the entry area where the light has
been introduced into the body is measured. Finally, an
5 estimate of the property to be monitored is determined from
the measured intensities of light leaving the body in the
first and second distance ranges from the entry area where the
light has been introduced into the body.

       According to this publication, reflectance pulse
10 oximetry and laser Doppler flowmetry are carried out as
separate independent measurements using an integrated sensor.
A signal generated by a second red light (660 nm) sensitive
photodiode, which is located twice as far away from the light
source as a first red light (660 nm) sensitive photodiode
15 (both photodiodes and the light source being positioned in
line), is used in addition to signals generated in response to
red and infrared light by the first red light sensitive
photodiode respectively the infrared light sensitive
photodiode. According to this publication, it was found
20 empirically that in an S_aO_2 range between 80 and 100 %,
readings from the thigh calculated with a calibration curve
obtained from readings from the forehead showed a reduced bias
and an improved precision if, instead of a mean intensity
signal of one red light photodiode, the difference between the
25 mean intensity signals of the first and the second red light
photodiodes is used in the calculation of the S_aO_2.

       There is however no empirical or theoretical evidence
with respect to the universal applicability of the calibration
curve, in particular at lower S_aO_2 levels.

30   Also the precision of the results of transmission pulse
oximetry at low S_aO_2 levels is relatively low when compared
with the precision at high S_aO_2 levels. In transmission pulse
oximetry the achieved precision is generally limited to 1.5 to
3 % at higher S_aO_2 levels (70-100 %), while at lower levels the
35 precision decreases and generally no measurement result is
obtained if the S_aO_2 values is below 50 %.

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A major factor determining the attainable precision is
is the pulse size. It has been found, that partly due to
relatively small pulse sizes, the precision of reflectance
pulse oximetry is not as good as the reported precision when
5   commercially available transmission pulse oximeters are used
(Dassel et al., 'Reflectance Pulse Oximetry in Fetal Lambs',
Pediatric Research, Vol. 31, No. 3, 1992).

Also in other noninvasive in-vivo measurement methods in
which light is passed through a part of the body of a living
10   human or animal body the problem occurs that optical
properties of the tissue and fluids in that part of the body
other than the properties to be measured influence the
measurement result. For instance the average Doppler frequency
measured during laser Doppler flowmetry, which provides an
15   indication of relative changes in blood flow - and in clinical
practice of the blood perfusion in tissue immediately below
the skin - is not only determined by the blood flow, but also
influenced by the optical properties of the tissue and the
blood which may vary between wavelength of the emitted light,
20   between individuals and also between different measurement
locations on the body. The known empirical method described
above does not provide for application in measurement
techniques other than reflectance pulse oximetry.

25   SUMMARY OF THE INVENTION

It is an object of the invention, to provide a more
precise method for estimating a property of a constituent of a
part of a human or animal body from optical measurements. More
30   in particular, it is an object of the present invention to
provide such a method in which optical characteristics of the
part of the body through which the detected light has
propagated or from which the detected light has been reflected
can be estimated and taken into account, in particular for
35   estimating S_aO_2 levels in reflectance pulse oximetry.

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According to the present invention, this object is achieved by measuring the intensities of introduced light of at least two of the wavelengths or wavelength ranges leaving the body in the second distance range from the entry area

5   where the light has been introduced into the body, and by using the measured intensities of the light of the two or more wavelengths or wavelength ranges in the second distance range from the entry area where the light has been introduced into the body for determining an estimate of the property to be

10 monitored.

According to the present invention, this object can also be achieved by measuring intensities of portions of the light of at least two of the wavelengths or wavelength ranges which has not been introduced into the body, and using the measured

15 intensities of the other portions of the emitted light for determining an estimate of the property to be monitored.

In each of these two methods according to the present invention, the intensities of light of each of the at least two, mutually different wavelengths or wavelength ranges

20 having travelled along different average path lengths through the body is detected. According to the first possibility, the position of one or more additional areas or light emitters is chosen in such a manner, that the second distance range is different from the first distance range. According to the

25 second possibility an additional detection area is positioned in such a manner that light reaching that area has not passed through the body, i.e. the average path length through the body is zero.

Methods according to the present invention can be used

30 for taking into account specific optical properties of the tissue and/or the blood and/or variations thereof in the calculation of estimates of the property to be monitored.

In particular, the method according to the present invention allows to differentiate between variation of the

35 absorption coefficient and the reduced scattering coefficient of the part of the body through which the detected light has

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propagated and therefore to design more universally applicable
and accurate calibration procedures. In experiments by the
inventor, in particular simultaneous calculation of an
estimate of the reduced scattering coefficient and taking into
5   account the estimated value thereof substantially improved the
precision of estimates of the S_aO_2 obtained by reflectance
pulse oximetry.

When used in combination with laser Doppler flowmetry,
the method according to the present invention can provide a
10 possibility to correct for the influence of both the
absorption coefficient and the reduced scattering coefficient
for the wavelength at which the laser Doppler flowmetry is
performed. Thus it is possible to correct for the tendency
that, at a given perfusion, the observed average Doppler
15 frequency is larger the lower the absorption coefficient and
the higher the scattering coefficient is, because the average
number of scattering events each detected photon has been
subjected to decreases with an increasing absorption
coefficient and increases with an increasing scattering
20 coefficient.

A further advantage of the method according to the
present invention is, that also correction factors for the
average penetration depth of detected light of each wavelength
or wavelength range become available. This is advantageous
25 where the assumption of a homogeneous change of the blood
volume fraction leads to unacceptable inaccuracies (e.g. if
pressure is applied to the probe or if measurements are taken
at the scalp).

Particular advantages of the mode of the method
30 according to the invention in which light leaving the body is
detected at at least two different distance ranges from the
area where the light has been introduced into the body are
that also pulsatile fluctuations in the reduced scattering
coefficient of arterial blood can be estimated and taken into
35 account, so that also variations of this factor can be allowed
for. Moreover, two different options to obtain estimates of

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this factor are made available. A first option is to calculate
the reduced scattering coefficient of arterial blood from
determined or default values of the hematocrit and/or the
plasma protein content. The second option is to calculate the
5   aforementioned factor by varying it, while keeping it
identical for both distance ranges, until the estimates of the
property to be monitored for both distance ranges are equal or
within a predetermined range of each other.

    Furthermore, the availability of relations between
10 intensities at different distance ranges for two wavelenghts
or wavelength ranges provides the possibility to statistically
analyze the noise contributions and to use the result thereof
to obtain better estimates of R_1/IR_1 and R_2/IR_2. Moreover, an
estimate of a measure of uncertainty such as a confidence
15 interval can be obtained.

    The invention can also be embodied in a device, a probe
or a driver/processor adapted for use in the measuring method
according to the present invention.

    Particular modes and embodiments of the invention are
20 set out in the dependent claims.

BRIEF DESCRIPTION OF THE DRAWINGS

    Fig. 1 is a block diagram of a device according to the
25 present invention,

    Fig. 2 is a schematic bottom view of a probe according
to the present invention,

    Figs. 3-5 are consecutive parts of a flow chart of an
algorithm for carrying out the present invention,

30   Fig. 6 is a schematic side view in cross-section of a
another probe according to the present invention, and

    Fig. 7 is a schematic bottom view of still another probe
according to the present invention.

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DETAILED DESCRIPTION OF THE BEST MODE AND VARIANTS OF THE
INVENTION

First, an example of a device for carrying out the
5 method according to the present invention and then an
algorithm for carrying out the method according to the
invention as such will be described.

Example of a device for carrying out the method according to
10 the invention

With reference to Fig. 1, the device generally consists
of a pulse oximetry driver/processor 1 and a probe 2 which is
shown in more detail in Fig. 2.
15   The probe 2 shown in Fig. 2, which represents the
presently most preferred embodiment thereof, has a diameter of
about 18 mm. It comprises a red and an infrared LED 3
respectively 4 (Cerled types CR 10 MR respectively CR 10 IR;
Electronic Consulting Services, Pfaffenhofen, Germany) for
20 emitting light at wavelengths about 660 nm respectively about
940 nm.
        The probe 2 further comprises a first and a second
detector in form of photodiodes 5 respectively 6 (Siemens BPW
32) of which the first detector 5 is closer to the LEDs than
25 the second detector 6. Each of the detectors is capable of
detecting light intensities at both wavelengths. The probe has
an internally black housing 7 to keep disturbing light away
from the entry area and the exit area of the patient's skin
where light is introduced into respectively received from the
30 part of the patient's body adjacent the probe 2. The
separation wall 8 between the LEDs 3, 4 and the detectors as
well as the inside of the probe 2 are also black to avoid
transmission of light which has not passed through the skin
from the LEDs to the detectors and to avoid re-entrance of
35 light into the body. The detectors 5, 6 and the LEDs 3, 4 have

been fixed by filling the housing 7 with clear epoxy resin
(e.g. EPOTEK 301).

The heart-to-heart distance between each of the LEDs 3,
4 and the first detector 5 is 4,8 mm. For the second detector
5   6 this distance is 7,4 mm. Preferably the largest LED to
detector distance should not be more than 8 to 9 mm, since at
greater distances apparently less reliable estimate of the
optical properties of the skin and therefore of the S_aO_2 have
been obtained. The maximum distance may also depend from the
10 location at the body of the patient against which the probe is
to be held. For use with animals other distances may be more
suitable. The distance of the LEDs 3, 4 to each of the
detectors 5, 6 is mutually equal, but may also be different
for example to achieve a more equal average penetration depth
15 of reflected light of the two wavelenghts. An equal
penetration depth is particularly important when measurements
are taken from parts of the body of which the structure varies
substantially with the depth beneath the skin, such as the
head.
20   The probe 2 is connected to the driver/processor 1 via a
cable 9. Means for cordless communication could be provided
instead.

The pulse oximetry driver analyzer 1 is to a large
extent identical to existing commercially available devices.
25   It comprises a housing 10. In this housing 10 are
provided a clock 11, which may for example provide a 2 Mhz
output signal, an EPROM 12 for controlling LED drivers 13 and
sample and hold circuits 14, amplifiers 15 interconnected with
the detectors 5, 6 for amplifying signals received from the
30 detectors 5 and 6. Preferably patient isolation according to
customary standards is also provided.

In operation, the signals received from the amplifier 15
are demultiplexed by the sample and hold circuit 14 where also
a constant signal caused by background illumination is
35 subtracted from the received signal.

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The driver/processor 1 further comprises logarithmic amplifiers 16, an analog/digital converter 17, a dataprocessor 18 and a display 19. Instead of or in addition to the display 19, a port for connecting display means such as a monitor or a
5 plotter to the driver/processor may be provided.

In operation, the signals received from the sample and hold circuit 14 are logarithmically amplified by the logarithmic amplifiers 16 so after amplification the fluctuations are proportional to the relative fluctuations of
10 the light intensities as detected. For determination of these relative fluctuations, signals are further amplified after high-pass filtering. The avareage intensities are derived from the unfiltered output of the logarithmic amplifiers 16. All the aforementioned signals are converted to digital values by
15 the analog/digital converter 17, for example into 12 bit digital values each 30 ms. The digital values are inputted into the dataprocessor 18, which calculates estimates of the optical properties and of a value for the S_aO_2 on the basis of the received signals and an algorithm.
20   Instead of using the shown driver/processor 1, the signals can also be processed in essentially the same manner or somewhat differently using a driver/processor with another structure. Essential functional differences between the driver/processor according to the present invention and known
25 driver/processors are, that the driver/processor according to the present invention is adapted for receiving and processing signals representing intensities of light of two or more wavelengths or wavelength ranges from two or more detectors (i.e. at least four different input signals) and programmed
30 for calculating an S_aO_2 value which is dependent from the relation between the signals generated by the different detectors.

The processor 18 is to be programmed on the basis of functions defining the relation between on the one hand the
35 intensities and ratios between the fluctuations of light of different wavelengths at different detectors and, on the other

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hand, optical properties of the part of the body in front of
the probe, tissue and/or the blood.

Monte Carlo simulations

5

Light propagation in turbid media - e.g. skin tissue and
blood - can be characterized by the following optical
characteristics: an absorption coefficient μ_a, a scattering
coefficient μ_s and a phase function which is the distribution
10 of scattering angles per scattering event.

The phase function is often characterized by the
asymmetry factor g, which is defined as the average cosine of
the scattering angles.

Predictions of light intensities at predetermined
15 detectors can be obtained by carrying out Monte Carlo
simulations for different values of the above-identified
optical characteristics.

Monte Carlo techniques for simulating light propagation
in turbid media are published in many earlier publications so
20 the skilled person will generally be familiar with these
techniques.

Nevertheless, for those who are not familiar with these
techniques, the principles of Monte Carlo techniques for
simulatiing light propagation in turbid media are set out
25 below.

The intensity decay of a collimated beam of photons in a
turbid medium equals the probability $p_t(z)$ that a photon has a
free path with a length z:

30
$$p_t(z) = \frac{I(z)}{I(0)} = \exp(-\mu_a z)\exp(-\mu_s z)$$
$$= \exp[-(\mu_a + \mu_s)\,z\,] = \exp(-\mu_t z). \tag{1}$$

35

$I(z)$ is the intensity at a distance z from the location where
the light enters the medium; μ_t is the transport coefficient.

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The chance that a photon travels within the collimated beam to a distance between z and z + dz can be found by differentiation of Eq. (1):

5   $p_t(z) - p_t(z + dz) = \mu_t \exp(-\mu_t z)dz.$ (2)

These photons can be absorbed or scattered. The scattered fraction equals:

10 $p_s(z) - p_s(z + dz) = \mu_s \exp(-\mu_t z)dz,$ (3)

which is a fraction c - which equals μ_s/μ_t - of the photons that leave the collimated beam. This fraction c is denoted as the "albedo".

15   The intensity decay of a collimated beam in a turbid medium has much in common with the free path length between interactions in Monte Carlo simulations. Therefore, in Monte Carlo simulations the distribution of photon path lengths resulting from Eq. (2) is simulated by choosing random values

20 for each free path length l_t between interactions of the photon during its course through the medium:

$$l_t = \frac{-1}{\mu_t} \ln(\varepsilon).$$ (4)

25

The Monte Carlo simulation comprises a repetition of the following sequence of steps. Firstly, a random number ε is picked between 0 and 1 to determine l_t. Secondly, a new random

30 number is ε is picked to determine whether the photon is absorbed or scattered. Thirdly, if the photon is scattered, then a scattering angle is picked from the phase function. If the photon has been absorbed simulation of the path of that photon is terminated. If the photon has not been absorbed, the

35 three step sequence set out above is repeated until the photon is absorbed or leaves the medium. Each time new random numbers ε are used. For reasons of efficiency, the photons may also be

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deemed to be absorbed if the number of interactions is very large, e.g. more than 20.000.

To determine whether the photon has been reflected or refracted at interfaces, the Fresnel law can be used by
5   picking a random number for each interaction to determine whether the photon is reflected or refracted.

Since Monte Carlo calculations require a substantial calculating effort, a condensed Monte Carlo simulation for semi-infinite media has been proposed in 'Condensed Monte
10 Carlo Simulations for The Description of Light Transport' by R. Graaff et al. in Applied Optics, Vol. 32, No. 4, pages 426-434, February 1993 the contents of which is hereby incorporated by reference.

The condensed Monte Carlo simulation described in that
15 publication essentially consists of using the results of one Monte Carlo simulation for modelling light propagation in a situation in which the albedo c, the scattering coefficient μ_s or the absorption coefficient μ_a are different from the corresponding value used in the original performed Monte Carlo
20 simulation.

Reliable results for the same value of μ_t but for values of the albedo c smaller than the albedo c_{sim} used in the original performed Monte Carlo simulation can be obtained quickly if from the original performed Monte Carlo simulation
25 the number of interactions within the simulated turbid medium N(i) has been stored for each photon path which has not been terminated by absorption of the photon. In that event the chance p(i) that a photon would have left a medium with an albedo c can be found for each photon using the following
30 equation:

$$p(i) = (c/c_{sim})^{N(i)}. \tag{5}$$

In a similar way, the average depth of all interactions
35 of detected photons can be calculated quickly if the average depth <d(1)> of each photon path has been stored too.

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If the simulated medium is semi-infinite and reflection from that medium is simulated, for each photon that has left the medium, the distance $r(i)$ from the place of entry where that photon is deemed to have left the medium must also be
5   available to determine the intensity in a predetermined area. If a slab has been simulated, it must furthermore be known for each photon that is deemed to have left the medium whether it is deemed to have been transmitted through the slab or to have been reflected back from the slab to determine the intensity
10 in a predetermined area at the front or the back side of the slab.

The use of results from a Monte Carlo simulation for modelling light transport in a medium having a different phase function (characterized by the average cosine of the
15 scattering angles g) than the phase function (characterized by g_{sim}) used in the Monte Carlo simulation is possible if similarity rules are applied, e.g. if it is assumed that if the absorption coefficients μ_a and the reduced scattering coefficients are mutually identical; i.e. if:
20

$$\mu_a = \mu_{a,sim}, \text{ and} \tag{6}$$

$$\mu_s' = \mu_s(1-g) = \mu_{s,sim}(1-g_{sim}), \tag{7}$$

25 the light distribution in the medium is the same in the simulation.

Similarity is not restricted to the range of validity of the diffusion theory, in which the reduced albedo $c' \approx 1$ ($c' \equiv \mu_s'/\mu_t'$). Similarity is also present if the reduced
30 albedo $c' \ll 1$, in particular if two media containing forward scattering particles are compared within the range $0,9 < g < 1$. Similarity can therefore be applied to scattering in biological media, e.g. the human skin, provided that the simulation is also performed with a phase function where
35 forward scattering dominates, i.e. with $g \approx 0,9$ or higher.

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The results from the condensed Monte Carlo simulations
are implemented in the algorithm embodied by the signal
processing software for each detector 5, 6 by determining a
function relating the intensities of received light to the
5   absorption coefficient μ_a and the reduced scattering
coefficient μ_s'. Preferably this is carried out by determining
coefficients of polynomials by fitting the polynomial to
results of Monte Carlo or condensed Monte Carlo simulations
for each detector separately. These polynomials are
10 independent from the wavelength and can for example be of the
following form:

$$\ln(I) = A_0 + A_1\mu_a + A_2(\mu_a)^{0,5} + A_3\mu_s' + A_4\ln(\mu_s') + A_5\mu_s'(\mu_a)^{0,5} + A_6\mu_s'^2.$$

$$(8)$$

15
From Eq. (8) derivatives

20 $$\xi_a = \frac{d\ln(I)}{d\mu_a} \quad \text{and} \quad \xi_s' = \frac{d\ln(I)}{d\mu_s'}$$

for each detector 5, 6 can be obtained for given values of μ_a
and μ_s'. For these properties fixed values can be used, but
25 estimates can also be obtained from in-situ measurements as is
described later.

The processor 18 of a driver/processor for carrying out
the method according to the invention is preferably programmed
to carry out the algorithm described below with reference to
30 Figs. 3-5.

Example of an algorithm for carrying out the method according
to the invention

35 I. Collection of light intensity data

The step denoted with reference numeral 20 (see Fig. 3)
comprises detecting and storing samples of the light
intensities for red and infrared light and for both the first

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and the second detector 3, 4. The samples are preferably taken
with a high frequency (e.g. each 30 ms) and over a time
interval which comprises at least one systole and diastole
cycle. If light of the two wavelengths is emitted in an
5 alternating sequence, values for different wavelengths of the
same sample can be detected one shortly after the other.
Instead of high frequency sampling, intensity values obtained
at systole and diastole may be selected.

       According to the presently most preferred mode of
10 carrying out the method according to the invention for
reflectance pulse oximetry, all measured intensities in a
certain time-interval are stored temporarily. Subsequently,
the intensity fluctuations are analyzed by means of linear
regression analysis using samples of the signals over a time
15 interval which is longer than the heart-beat cycle. The data
denoted by $\ln[I_i(R)]$ and $\ln[I_i(IR)]$ are used for obtaining
ratios between intensities detected at different distances
from the source. The data denoted by $\Delta\ln[I_i(R)]$ and $\Delta\ln[I_i(IR)]$
are used to analyze the intensity fluctuations. The latter
20 data are obtained after high-pass (e.g. 0.6 Hz) filtering and
additional amplification of the signal (e.g. 20 times).

       From the measurement results, estimates of the optical
properties of the portion of the body in front of the probe 2
are calculated as is set forth below.
25

II. Estimation of optical properties of a part of the body

       The ratio between the average intensities at the two
detectors 5 and 6 are calculated from the stored values of
30 $\ln[I_i(R)]$ and $\ln[I_i(IR)]$ as is denoted by steps 21 and 22.
Subsequently, the polynomials of the structure of Eq. (8) are
used inversely to calculate the reduced scattering coefficient
$\mu_s'(IR)$ from the ratio between the intensities at detectors 1
and 2, for example with an assumed non-pulsatile value for
35 $\mu_a(IR)$ of 0.035 mm^{-1} as denoted by steps 23 and 24 (see
Fig. 3).

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According to step 25 a fixed ratio between the reduced
scattering coefficients of the total medium at the two
wavelengths or wavelength ranges is assumed, for example
$\mu_{s,t}'(IR) / \mu_{s,t}'(R) = 0.53$ (cf. Table 8 of 'Optical properties
5   of human dermis in-vitro and in-vivo', R. Graaff et al.,
Applied Optics, Vol. 32 No. 4, February 1993, pages 435-447).
        Values of the pulse independent part of the reduced
scattering coefficients for infrared light can then be
determined as denoted by step 26. Subsequently, the inverse
10 algorithm using Eq. (8) is used to determine $\mu_a(R)$ from $u_s'(R)$
and $I_2/I_1(R)$ as denoted by step 27. Thus estimates of the
optical properties of the medium have been obtained for both
wavelengths.

15 III. Analysis of intensity fluctuations

        Signal processing of the intensity fluctuations can be
performed in several ways. The optimal choise depends on many
aspects, for instance, the signal to noise ratio of the
20 signals at each detector, and whether the LEDs generate
secondary emissions at other wavelengths.
        The analysis for each wavelength (λ) and each detector 5,
6 (i) is based on equations as given below. It is noted that
in the equations i = 1 denotes the detector 5 closest to the
25 light sources 3, 4 and i = 2 denotes the remote detector 6.

$$\Delta\ln[I_i(\lambda)] = \xi_{a,i}(\lambda) \; \Delta\mu_a(\lambda) + \xi_{s,i}'(\lambda) \; \Delta\mu_s'(\lambda)$$
$$= [\xi_{a,i}(\lambda) + \xi_{s,i}'(\lambda) \; F(\lambda)] \; \Delta\mu_a(\lambda) \qquad (9)$$

30 with

$$F(\lambda) = \frac{\mu_{s,a}'(\lambda) \; \chi - \mu_s'(\lambda)}{\mu_{a,a}(\lambda) - \mu_a(\lambda)}, \qquad (10)$$

35

where $\xi_{a,i}(\lambda)$ and $\xi_{s,i}'(\lambda)$ are the derivatives that are obtained
in step 29 using Eq. (8) with the coefficients of the

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respective detector 1 and 2 (5 and 6, respectively in Fig. 2). The terms $\mu_a(\lambda)$ and $\mu_s'(\lambda)$ are the absorption coefficient respectively the reduced scattering coefficient of the part of the body in front of the probe for wavelength λ, as determined in steps 21-28. The values $\mu_{a,a}(\lambda)$ and $\mu_{s,a}'(\lambda)$ are the absorption coefficient respectively the reduced scattering coefficient of arterial blood. The multiplier χ is optional (default value = 1); the meaning of it is discussed below.

The variations $\Delta\mu_a(\lambda)$ and $\Delta\mu_s'(\lambda)$ can also be obtained from a linear combination of $\Delta\ln[I_1(\lambda)]$ and $\Delta\ln[I_2(\lambda)]$. However, a somewhat different procedure is followed in the present algorithm.

In step 31 the absorption coefficients for oxygenated and de-oxygenated blood are calculated using input values determined in step 30 and the equations (11) and (12) set out below.

$$\mu_{a,a,oxy}(\lambda) = \frac{c_{t,Hb}}{150} \{2.12(1-f_{HbCo}-f_{Hi}) \in_{HbO2}(\lambda) + f_{Hi} \in_{HbCo}(\lambda) + f_{Hi} \in_{Hi}(\lambda)\} + f_{a,H2O} \mu_{a,H2O}(\lambda) \qquad (11)$$

and

$$\mu_{a,a,de-oxy}(\lambda) = \frac{c_{t,Hb}}{150} \{2.12(1-f_{HbCo}-f_{Hi}) \in_{Hb}(\lambda) + f_{Hi} \in_{HbCo}(\lambda) + f_{Hi} \in_{Hi}(\lambda)\} + f_{a,H2O} \mu_{a,H2O}(\lambda) \qquad (12)$$

In these equations (11) and (12), $\in_{Hb}(\lambda)$, $\in_{HbO2}(\lambda)$, $\in_{HbCo}(\lambda)$ and $\in_{Hi}(\lambda)$ are the extinction coefficients of de-oxyhemoglobin, oxyhemoglobin, carboxyhemoglobin, and methemoglobin, respectively. Furthermore, f_{HbCo} and f_{Hi} are the molar fractions of carboxyhemoglobin and methemoglobin in the blood, and $f_{a,H2O}$ and $\mu_{a,H2O}(\lambda)$ are the volume fraction of water in blood - for instance assumed to be $f_{a,H2O} = 0.90$ - respectively the absorption coefficient of water at wavelength λ. Finally, $c_{t,Hb}$ is the total hemoglobin content of the blood in g/L.

The total hemoglobin content $c_{t,Hb}$ as well as the fractions HbCo and Hi can be determined in step 30.

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Alternatively, default values can be used for one, two or all of these three variables, for instance $c_{t,Hb} = 150$ g/L, $f_{HbCO} = 0$ and $f_{Hi} = 0$.

According to the present algorithm, the reduced
5   scattering coefficients of arterial blood at each of the applied wavelengths only depend on the total hemoglobin content, which is obtained from step 30. To determine the reduced scattering coefficient of blood, as denoted by step 32, for instance the following relation may be used:

10

$$\mu_{s,a}'(660 \text{ nm}) = 10.8 \text{ H} (1 - \text{H}) (1.4 - \text{H}) M_{pl}$$

(13)

where H is the hematocrit with $H = 0.0030 \ c_{tHb}$. M_{pl} is a
15 correction factor for the individual refractive index of blood plasma n_{pl} which is influenced by the plasma protein content. This relation can be described as follows:

20 $$M_{pl} = [(\frac{1.4}{n_{pl}} - 1) \ / \ [(\frac{1.4}{n_{avg}} - 1)]^{2.09},$$

where n_{avg} is the normal refractive index of blood plasma. The reduced scattering coefficient at other wavelengths can for
25 instance be calculated using the following equation:

$$\mu_{s,a}'(\lambda_1)/\mu_{s,a}'(\lambda_2) = (\lambda_1/\lambda_2)^{-0.37}.$$ (14)

R_1/IR_1 and R_2/IR_2, R_1/R_2 and IR_1/IR_2 are calculated from
30 the light intensity data stored in step 20. The calculated ratios are stored as set out in steps 33-36. All values may be obtained in a similar way as in commercially available pulse oximeter devices, for instance by analysis of the difference between minimum and maximum. In the present algorithm the
35 slopes obtained by linear regression analysis of the light intensity data are used as is described below. Thereby, it is possible to use the whole signal or to select the inclinations and/or declinations during the systolic parts of the

registrations, depending on the accuracy in the predicted
saturation that can be obtained.

First estimates for R_1/IR_1 and R_2/IR_2 for each detector
separately are obtained from the slopes $b_{R1.IR1}$, $b_{IR1.R1}$,
5   $b_{R2.IR2}$, and $b_{IR2.R2}$ in a linear regression analysis, where the
data of $\Delta ln[I(\lambda_1)]$ and $\Delta ln(I(\lambda_2)]$ are the independent variable
by turns as denoted by step 33. Correlation coefficients and
variances are also calculated.

Similarly, $b_{R1.R2}$, $b_{R2.R1}$, $b_{IR1.IR2}$, and $b_{IR2.IR1}$ are the
10 first estimates for R_1/R_2 and IR_1/IR_2 that are obtained in step
34, where the data of $\Delta ln[I_1(\lambda)]$ and $\Delta ln(I_2(\lambda)]$ are the
independent variable by turns. Correlation coefficients and
variances are also calculated.

The correlation coefficients and variances from step 33
15 and 34, which also denote the 'lack of correlation' for each
detector, are used in step 35 for estimation of the
contributions of uncorrelated signal by each of the signals,
since the correlations between the red and infrared signals
are not only determined by the arterial volume fluctuations,
20 but for instance also by noise and venous volume fluctuations,
which may differ for each of the input signals. For modelling
the relation between the variances and the correlation
coefficients, equations of the following form can be used:

25   $$R^2_{R1,IR1} = (1 - \frac{\delta^2_{R1}}{\sigma^2_{R1}} - \frac{\delta^2_{R1,v}}{\sigma^2_{R1}}) \; (1 - \frac{\delta^2_{IR1}}{\sigma^2_{IR1}} - \frac{\delta^2_{IR1,v}}{\sigma^2_{IR1}}) \qquad (15)$$

where σ^2_{R1} and σ^2_{IR1} are the (total) variances of each signal,
30 $\delta^2_{R1,v}$ and $\delta^2_{IR1,v}$ are uncorrelated parts of the variance caused
by venous volume fluctuations, and δ^2_{R1} and δ^2_{IR2} are the
uncorrelated parts of the remaining variances. The
uncorrelated part of the variance can be evaluated when it is
assumed, firstly, that venous volume fluctuations do not alter
35 the uncorrelated parts of the two signals obtained with the
same wavelength, secondly, that the ratio between the
remaining red and infrared noise amplitudes is the same for
each detector, and, thirdly, that for each wavelength the

ratio between the venous and arterial variances, for instance $\delta^2_{R1,v}/(1-\sigma^2_{R1})$, has the same value for both detectors. From these assumptions it can be concluded that the venous terms of the variance are absent in equations similar to Eq. (15) for

5   determining the correlations between signals for the same wavelength at different detectors, as denoted by step 34. Moreover, the ratio $R^2_{R1,IR1}/R^2_{R2,IR2}$ does not depend on the venous terms in that case. The remaining terms $\delta^2_{R1}...\delta^2_{IR2}$ are solved using these assumptions.

10   Subsequently, better estimates for the slopes, denoted by $b'_{R1.IR1}$ etc., can be calculated as step 35 using equations of the form

$$15 \quad b'_{R1.IR1} = \frac{b_{R1.IR1}}{1 - \dfrac{\delta^2_{IR1}}{\sigma^2_{IR1}}}. \qquad\qquad (16)$$

20

The slopes for the values of R_1/R_2 calculated in this way are equal, $R_1/R_2 = b'_{R1.R2} = 1/b'_{R2.R1}$. This principle also applies for the slopes for IR_1/IR_2. The corrected slopes for the correlations between the red and infrared intensity

25   fluctuations generally remain different, since none of the red and infrared signals can be considered to be independent. Therefore, the values R_1/IR_1 and R_2/IR_2 that have to be obtained are generally between both pairs of slopes, respectively. The estimate of the arterial oxygen saturation

30   can, for instance, be calculated from the bisector between each pair of slopes.

IV. Determination of S_aO_2 from the linear regression results

35   *a. if a homogeneous distribution of arterial volume fluctuations is assumed*

Finally, the arterial oxygen saturation can be determined from the regression results. If the pulsations are

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assumed to be distributed homogeneously over the medium this
is performed with equations having the structure of Eq. (9):

$$R_1/IR_1 = \frac{dln[I_1(R)]/df_a}{dln[I_1(IR)]/df_a}$$

$$= \frac{\xi_{a,1}(R)\ d\mu_a(R)/df_a + \xi_{s,1}'(R)d\mu_s'(R)/df_a}{\xi_{a,1}(IR)\ d\mu_a(IR)/df_a + \xi_{s,1}'(IR)d\mu_s'(IR)/df_a} \qquad (17)$$

and corresponding equations for R_2/IR_2, R_1/R_2 and IR_1/IR_2. The
differential terms represent changes in the absorption and
reduced scattering coefficients caused by changes in the
arterial blood volume fraction f_a:

$$d\mu_a(\lambda)/df_a = \mu_{a,a}(\lambda) - \mu_a(\lambda) \qquad (18)$$

$$d\mu_s'(\lambda)/df_a = \mu_{a,s}'(\lambda)\ \chi - \mu_s'(\lambda). \qquad (19)$$

The coefficients ξ_a and ξ_s' are obtained from step 29.
Eq. (19) shows that a value for the multiplier χ different
from 1 may be given to correct for deviations from the assumed
values. Such deviations may for example be caused by
differences between the assumed and the actual plasma protein
concentrations. The multiplier χ will then have the same value
for all wavelengths. The default value for χ is one (1).

The multiplier χ may also be determined from the
measured values of R_1/R_2 or IR_1/IR_2. In principle both results
give the same value for χ. If determined in this manner, χ
corrects for deviations in the reduced scattering
coefficients, but also for changes in the reduced scattering
coefficient of blood during the pulsations, which may for
example be caused by changes in red cell aggregation.

The only unknowns in Eqs. (17) to (19) are the
absorption coefficients of the arterial blood. From Eq. (11)
and (12) it follows that the absorption coefficients of blood
at each wavelength are linearly related to the arterial oxygen
saturation that has to be determined:

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$$\mu_{a,a}(\lambda) = \mu_{a,a,de-oxy}(\lambda) + (S_aO_2/100\%)\ \mu_{a,a,oxy}(\lambda) \qquad (20)$$

After substitution of Eqs. (18) to (20) into Eq. (17)
5 the arterial oxygen saturation can be solved, since S_aO_2 is
linearly related with R_1/IR_1 in Eq. (17). Substitution of the
saturation into the equations for R_1/R_2, IR_1/IR_2 and R_2/IR_2
will give agreement with the measured values, provided that
the value for χ is chosen correctly, and the arterial blood
10 volume fluctuations are in fact distributed homogeneously
within the part of the body from which the measurements were
or are taken.

b. if a homogeneous distribution of arterial blood is not
15 *assumed*

The presence of blood vessels may also influence R/IR if
a fraction of the light pulsations is determined by blood
within vessels of which diameters are not small compared to
20 $1/\mu_{s,a}'(\lambda)$ or $1/\mu_{a,a}(\lambda)$. In that event the changes $d\mu_a$ and $d\mu_s'$
of the optical properties of the medium cannot be interpreted
with Eqs. (18) and (19).
     However, light propagation through blood contained in a
vessel can be modelled by considering interaction with a blood
25 vessel as a single interaction. Values for apparent properties
for this single interaction can be obtained from (condensed)
Monte Carlo simulations of diffusely illuminated cylindrical
blood vessels as a function of $\mu_{a,a}d$ or $\mu_{s,a}'d$. From these
simulations, the apparent chance of absorption during
30 interaction $1-c_{a,App}$ can be calculated as well as an apparent
average cosine of the scattering angle for this interaction
$g_{a,App}$.
     Pulsations can then me modelled as changes in the
diameter of the blood vessel, which will influence the
35 apparent absorption and reduced scattering coefficients.

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It is to be taken into account, that the reduced
scattering coefficient is influenced by the absorption
properties of blood, whereas in the model in which the medium
is assumed to be homogeneous, the reduced scattering
5 coefficient is not influenced by the absorption properties of
blood.

*c. if a layered distribution of arterial volume fluctuations
is assumed*
10

Differences between the light paths of red and infrared
light may introduce complications in the determination of S_aO_2
if the arterial blood volume fluctuations are a function of
depth below the skin surface. In that case the results
15 calculated with an assumed homogeneous distribution of blood
pulsations will be biased. However, since the average depths
of the photon paths to the detector 6 (denoted by $_2$ in the
equations) remote from the light source into the body are
larger than for the photon paths to the detector 5 (denoted by
20 $_1$ in the equations) nearer to the light source, a correction
algorithm can be used to allow for the differences between the
average depths of the photon paths of photons reaching the
different detectors 5 and 6. This can be performed by using a
linear combination of the intensity fluctuations at detectors
25 5 and 6 for one of the wavelengths, and calculate the arterial
oxygen saturation for instance from:

$$
30 \quad \frac{R_2/IR_2}{1+A_1\ IR_1/IR_2} = \frac{R2}{IR_2+A_1\ IR_1} = \frac{d\ln[I_2(R)]/df_a}{d\ln[I_2(IR)]/df_a+A_1d\ln[I_1(IR)]/df_a}
$$

$$(21)$$

An empirically derived value of A_1, for instance
35 $A_1 = .1.1$, can be used in the algorithms to derive S_aO_2. It is
noted that Eq. (21) reduces to Eq. (17) if $A_1 = 0$. An equation
similar to Eq. (21) can be given based on the values for R_1/IR_1
and IR_1/IR_2 with an empirical value for A_2, which differs from
the value for A_1. The saturations derived with both equations

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will be the same, if the value for χ has been estimated correctly. Therefore, the results can also be used to derive a value for χ or to obtain a second estimate for this multiplier as will be described below.

5   Another option - provided for in the algorithm shown in the drawings - is to determine the values for A_1 and/or A_2 from (condensed) Monte Carlo simulation data, based on the principle that the average depth from which the signal contributions occur should be equal for both wavelengths. To

10   derive the average depths for each detector from condensed Monte Carlo simulations it is necessary that the average depth for each photon path, $d[i]$ has been stored. The average depth of all detected photons as a function of μ_a and μ_s' can then be obtained from

15

$$<D> = \frac{<d[i]\ p[i]\ N[i]>}{<p[i]\ N[i]>}. \tag{22}$$

20

The number of interactions $N[i]$ has been inserted in the weight function to correct for the size of the contribution which is proportional to the path length, or $N[i]$. For the use of $<D>$ in the determination of A_1 the results for $<D>$ can be

25   described by polynomials which have been designed in a similar way as Eq. (8) by fitting the Monte Carlo data of $<D>$ as a function of μ_a and μ_s' for each detector. This method is applied in step 37.

In step 38 the values for A_1 and A_2 are derived. The

30   correction for the influence of depth dependent fluctuations of the arterial volume fraction for the red signal at the second detector 6 is obtained with

35     $$<D_2(R)> = \frac{<D_2(IR)> + A_1\ IR_1/IR_2\ <D_1(IR)>}{1 + A_1\ IR_1/IR_2}, \tag{23}$$

which gives the value of A_1. A similar equation can be solved

40   for the red light received at the detector 5 nearest to the light source which gives A_2.

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With the obtained values for A_1 and/or A_2 the oxygen saturation(s) are derived as is denoted by step 40. For the results of R_2/IR_2 and IR from step 36 the combination of Eqs. (17) and (23) yields

$$\frac{R_2/IR_2}{1 + A_1 \, IR_1/IR_2} =$$

$$\frac{\xi_{a,2}(R) \, d\mu_a(R)/df_a + \xi_{s,2}'(R) \, d\mu_s'(R)/df_a}{[\xi_{a,2}(IR)+A_1\xi_{a,1}(IR)]d\mu_a(IR)/df_a+[\xi_{s,2}'(IR)+A_1\xi_{s,1}(IR)]d\mu_s'(IR)/df_a} \, . \quad (24)$$

After substitution of Eqs. (18) to (20) into Eq. (24) the relation between S_aO_2 and the lefthand term in Eq. (24) is found. S_aO_2 is calculated using this relation in step 40. Substitution of the saturation into a similar equation based on R_1/IR_1 and the corresponding constant A_2 will give agreement with the measured values provided that the value for χ is chosen correctly. The initial value of χ can be a fixed default value or be specified - for example obtained from Eq. (19) - as denoted by step 39.

In step 41 it is checked whether the S_aO_2 calculated with A_2 is within a predetermined tolerance range about the S_aO_2 value calculated for A_1. If the value calculated for A_2 is outside that tolerance range, then at step 43 the value of χ is varied, the new value is read in step 39 and the calculations of step 40 are repeated with that new value of χ. The cycle of steps 38-41 and 43 is repeated until the value calculated with A_2 is within the specified tolerance range. Then the S_aO_2 estimate is displayed with the corresponding measure of uncertainty (step 42).

Alternatively, the most likely value for S_aO_2 can be calculated from the two estimated values for the S_aO_2 and the uncertainties in these properties.

<u>Alternative modes and embodiments of the invention</u>

Within the framework of the present invention many other alternatives will be apparent to the skilled person, both

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regarding the hardware for carrying out the method as
regarding modes for carrying out the method.

   In the shown algorithm many steps may be carried out in
a different order. For example the step 37 in which the
5   average penetration depth is determined may be carried out
immediatley after the μ_a and μ_s' have become available from
step 28. Furthermore, for example steps 33 to 36, in which the
relations between relative fluctuations at different distance
ranges and different wavelengths or wavelength ranges are
10 analyzed, can be carried out immediately after the measuring
step 20 and before analysis of the avarage intensities in
steps 21 to 29.

   It is also possible to leave out one or more steps. For
example where the direct comparison of light intensities
15 detected at different detectors is not reliable - this occurs
for example if measurements are taken from the fetal scalp
during labour, because of the possible presence of hair,
meconium, and vernix in front of one or more of the
detectors - it is generally more reliable to use assumed
20 values for μ_a and μ_s' so the steps 21-28 can be replaced by
entering assumed or default values. It is noted that the
measurement of relative fluctuations is not affected by the
presence of obstacles in front of one or more of the detectors
as long as sufficient light reaches the detectors. Measurement
25 of the hematocrit and hemoglobin fractions will generally not
appear opportune where normal values can be expected. In such
situations steps 30 and 31 can be replaced by enetering
assumed or default values.

   In Fig. 6 another probe according to the invention, is
30 shown in a position against a body 110. This probe comprises
two LEDs 103, 104, a first detector 105 and a second detector
106. The second detector is positioned at the side of the LEDs
facing away from the side of the probe which is to be held
against the skin. Connection 109 comprises individual
35 connections for each detector 105, 106 and for each LED 103,
104. Instead of for determining the ratio between light at

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different distances from the source, this probe is adapted for
determining the ratio between light which has propagated
through the skin and light which has reached the detector 106
without propagating through the skin. Relations between that
5 ratio and values of μ_a and μ_s' can be provided, so μ_a and μ_s'
can be determined for each wavelength using these ratios.
These ratios can also be used in addition to ratios between
light intensities at different distance ranges from the light
source, so that less assumptions are needed and more
10 variations of optical properties can be taken into account.

In Fig. 7 still another probe according to the present
invention is shown. In this probe two detectors 204 and 205
are provided. Detector 204 is adapted for detecting red light
and detector 205 is adapted for detecting infrared light. For
15 emitting red light LEDs 201, 202 at diferent distances from
the detector 204 are provided. For emitting infrared light
LEDs 200, 203 at diferent distances from the detector 205 are
provided. Alternating operation of on the one hand the LEDs
202, 203 close to the detectors 204, 205 and, on the other
20 hand, the LEDs 200, 201 remote from the detectors 204, 205,
provides the possibility to measure intensities of light
leaving the body at different distances from the area where
the light has been introduced into the body.

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CLAIMS

1. A method for noninvasively, in-vivo monitoring a
property of a constituent of a human or animal body comprising
the actions of:
     introducing light of at least two, mutually different
5 wavelengths or wavelength ranges through at least one entry
area into the body,
     measuring intensities of light of each of said
wavelengths or wavelength ranges leaving the body in a first
distance range from the entry area where the light has been
10 introduced into the body,
     measuring an intensity of light of a wavelength or
wavelength range leaving the body in a second distance range
from the entry area where the light has been introduced into
the body, and
15   determining an estimate of the property to be monitored
from the measured intensities of light leaving the body in
said first and second distance ranges from the entry area
where the light has been introduced into the body,
     characterized by:
20   measuring the intensities of introduced light of at
least two of said wavelengths or wavelength ranges leaving the
body in said second distance range from the entry area where
the light has been introduced into the body, and
     using said measured intensities of the light of said at
25 least two wavelengths or wavelength ranges in said second
distance range from the entry area where the light has been
introduced into the body for determining an estimate of the
property to be monitored.
     2. A method according to claim 1 in which, for each of
30 at least two of said wavelengths or wavelength ranges, the
ratio between intensities of the light leaving the body in
said first and second distance ranges from the entry area is
calculated.

3. A method according to claim 1 or 2 in which, for a number of samples and each of at least two of said wavelengths or wavelength ranges, ratios between relative intensity fluctuations of the light leaving the body in said first and
5   second distance ranges from the entry area are calculated, noise contributions are determined and ratios are corrected using these noise contributions.

4. A method according to any one of the preceding claims in which an estimate of the reduced scattering coefficient of
10 arterial blood and changes thereof are calculated from a ratio of relative fluctuations of light of the same wavelength or wavelength-range at different distance ranges from the area where the light has been introduced into the body.

5. A method according to any one of the preceding claims
15 in which a common multiplier representing changes in the reduced scattering coefficient of blood in estimates of the S_aO_2, obtained from measurements at different distance ranges from the entry area where the light has been introduced into the body, is varied until a value for this multiplier is found
20 for which one of these estimates is within a predetermined tolerance range around the other estimate.

6. A method for noninvasively, in-vivo monitoring a property of a constituent of a human or animal body comprising the actions of:
25   emitting light of at least two, mutually different wavelengths or wavelength ranges,
        introducing at least a portion of said light through at least one entry area into the body,
        measuring intensities of light of each of said
30 wavelengths or wavelength ranges leaving the body in a distance range from the entry area where the light has been introduced into the body, and
        using said intensities measured at said distance range from the entry area where the light has been introduced into
35 the body for determining an estimate of the property to be monitored,

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characterized by:

measuring an intensity of other portions of the light of at least two of said wavelengths or wavelength ranges which have not been introduced into the body, and

5   using the measured intensities of said other portions of the emitted light for determining an estimate of the property to be monitored

7. A method according to claim 6 in which, for each of at least two of said wavelengths or wavelength ranges, the

10   ratio between intensities of the light leaving the body in said distance range from the entry area and said other portion of light is calculated.

8. A method according to any one of the preceding claims in which relations between light intensities detected at each

15   of said different areas and estimates of optical properties of the body are provided and at least one of said optical properties is determined by comparing the intensities of light of the same wavelength leaving the body at different distance ranges from the area where the light has been introduced into

20   the body.

9. A method according to claim 8 in which these relations are provided in form of polynomials of which variables represent the optical properties.

10. A method according to claim 8 in which these

25   relations are provided in form of sets of coordinates in an at least three dimensional space.

11. A method according to any one of the preceding claims in which correction factors for the average penetration depth of light leaving the body in each of said distance

30   ranges from the area where the light has been introduced into the body are provided for each wavelength or wavelength-range.

12. A method according to any one of the preceding claims in which the light of which the intensities are measured leaves the body through surfaces facing in

35   essentially the same direction as the entry areas through which that light has been introduced into the body.

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13. A device for carrying out a method according to any one of the preceding claims comprising a probe (2) and a pulse oximetry driver/processor (1) connected to that probe,

said probe (2) comprising cooperating light emitting
5 means (3, 4; 103, 104; 200, 201, 202, 203) and light detector means (5, 6; 105, 106; 204, 205) positioned at different mutual spacings, said light emitting means (3, 4; 103, 104; 200, 201, 202, 203) and said light detector means (5, 6; 105, 106; 204, 205) being adapted for emitting respectively
10 receiving light of at least two, mutually different wavelengths or wavelength ranges, and

said driver/processor (1) comprising signal processing means (15-18) adapted for determining an estimate of a property to be monitored from signals representing light
15 intensities of at least two wavelengths or wavelength ranges received from light emitting means (3, 4; 103, 104; 200, 201, 202, 203) differently spaced from the detector means (5, 6; 105, 106; 204, 205) from which the signals are received, means for communicating signals from the light detector means (5, 6;
20 105, 106; 204, 205) to the signal processing means (15-18), and display means (19) or a port for connecting such display means connected to said signal processing means (15-18).

14. A probe for use in the method according to any one of the claims 1-12 comprising cooperating light emitting means
25 (3, 4; 103, 104; 200, 201, 202, 203) and light detector means (5, 6; 105, 106; 204, 205) positioned at different mutual spacings, said light emitting means (3, 4; 103, 104; 200, 201, 202, 203) and said light detector means (5, 6; 105, 106; 204, 205) being adapted for emitting respectively receiving light
30 of at least two, mutually different wavelengths or wavelength ranges.

15. A probe according to claim 14 in which the light detector means comprise detectors (5, 6) or sets of detectors positioned at mutually different distances from the light
35 emitting means (3, 4), each detector of set of detectors being connected to an individual associated communication line.

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16. A probe according to claim 14 in which the light
emitting means comprise light emitters (200, 201, 202, 203) or
sets of light emitters positioned at mutually different
distances from the light detector means (204, 205), each
5 emitter (200, 201, 202, 203) or set of emitters being
connected to an individual associated power supply line for
alternating operation of that emitter (200, 201, 202, 203) or
set of emitters.

17. A probe according to claim 14 in which the light
10 detector means comprise detectors (105, 106) or sets of
detectors positioned in mutually different directions from the
light emitting means (103, 104) such that at least one of said
detectors or sets of detectors is positioned for directly
receiving a portion of the light emitted by the light emitting
15 means, each detector or set of detectors being connected to an
individual associated communication line.

18. A probe according to any one of the claims 14-17, in
which the emitting surfaces of light emitting means (3, 4;
103, 104; 200, 201, 202, 203) and the receiving surfaces of
20 the light detectors (5, 6; 105, 106; 204, 205) are facing in
essentially the same direction.

19. A pulse oximetry driver/processor for use in the
method according to one of the claims 1-12, comprising
signal processing means (15-18) adapted for determining
25 an estimate of a property to be monitored from signals
representing light intensities of at least two wavelengths or
wavelength ranges received from light emitting means (3, 4;
103, 104; 200, 201, 202, 203) differently spaced from the
detector means (5, 6; 105, 106; 204, 205) from which the
30 signals are received,
means for communicating signals from the light detector
means (5, 6; 105, 106; 204, 205) to the signal processing
means (15-18), and
display means (19) or a port for connecting such display
35 means connected to said signal processing means (15-18).

FIG. 1

FIG. 2

FIG. 6

FIG. 7

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┌─────────────────────────────────────────────┐
│        Detect and store n samples of         │
│ ln [I₁(R)], ln [I₂(R)], ln [I₁(IR)], ln [I₂(IR)], │──── 20
│ Δln [I₁(R)], Δln [I₂(R)], Δln [I₁(IR)], Δln [I₂(IR)] │
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│           Calculate average values of         │──── 21
│   ln [I₁(R)], ln [I₂(R)], ln [I₁(IR)], ln [I₂(IR)] │
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│            Calculate ratios of averages        │──── 22
│       I₂(R) / I₁(R) and I₂(IR) / I₁(IR)        │
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│         Read assumed value for μa(IR)         │──── 23
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│  Determine μs'(IR) using Eqs. (8) for each detector and │──── 24
│             value I₂(IR) / I₁(IR)             │
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│       Read assumed value for μs'(IR) / μs'(R)       │──── 25
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│   Determine μs'(R) from μs'(IR) / [μs'(IR) / μs'(R)]   │──── 26
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│  Determine μa(R) using Eqs. (8) for each detector and  │──── 27
│              value I₂(R) / I₁(R)              │
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│      Store μa(R), μa(IR), μs'(R), μs'(IR)       │──── 28
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│ Determine ξa,1(R), ξa,2(R), ξs,1'(R), ξs,2'(R), ξa,1(R), │──── 29
│  ξa,2(IR), ξs,1'(IR), ξs,2'(IR) using Eqs. (8)  │
└─────────────────────────────────────────────┘
                      │
                      ▼ to 30
```

$$\textbf{FIG. 3}$$

from 29

↓

| Read values for $C_{t,Hb}$, f_{HbCo}, f_{Hi} or read default values $C_{t,Hb}$ = 150 g/l, f_{HbCo} = 0, f_{Hi} = 0 | 30 |

↓

| Determine absorbtion coefficients of oxygenated and de-oxygenated blood $\mu_{a,a,oxy}$ (R), $\mu_{a,a,oxy}$ (IR) resp. $\mu_{a,a,de-oxy}$ (R), $\mu_{a,a,de-oxy}$ (IR) using Eqs. (11) and (12) | 31 |

↓

| Determine scattering coefficients of blood $\mu_{s,a}'$(R), $\mu_{s,a}'$(IR) from $C_{t,Hb}$ using Eqs. (13) and (14) | 32 |

↓

| Determine slopes $b_{x.y}$ and $b_{y.x}$, variances and correlation coefficients between: $\Delta\ln [I_1(R)]$ and $\Delta\ln [I_1(IR)]$ $\Delta\ln [I_2(R)]$ and $\Delta\ln [I_2(IR)]$ | 33 |

↓

| Determine slopes $b_{x.y}$ and $b_{y.x}$, variances and correlation coefficients between: $\Delta\ln [I_1(R)]$ and $\Delta\ln [I_2(R)]$ $\Delta\ln [I_1(IR)]$ and $\Delta\ln [I_2(IR)]$ | 34 |

↓

| Determine noise contributions using Eq. (15) and determine corrected slopes $b_{x.y}$ and $b_{y.x}$ for each relation with Eq. (16) | 35 |

↓

| Calculate R_1/IR_1, R_2/IR_2, R_1/R_2, IR_1/IR_2 and measure of uncertainty | 36 |

↓ to 37

FIG. 4

5/5

from 36

Determine <D> for each detector and for each
wavelength using Eq. (22) and Monte Carlo results   ⌐ 37

Determine A_1 using Eq. (23) and determine A_2
similarly   ⌐ 38

Read χ; default value $\chi = 1$ ⌐ 39

Determine:
$SaO_2(1)$ using Eqs. (18) -(20) and (24) with A_1,
$SaO_2(1)$ using Eqs. (18) -(20) and (24) with A_2, and
measures of uncertainty for SaO_2 (1) and $SaO_2(2)$ ⌐ 40

$SaO_2(1) = SaO_2(2)$ yes

no   41

Determine new value for χ ⌐ 43

Display:
SaO_2 estimate,
measure of uncertainty for SaO_2 ⌐ 42

FIG. 5

INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6   A61B5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6   A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO,A,93 11701 (VIVASCAN CORP.) 24 June 1993	1,2, 12-15, 18,19
Y	see the whole document ---	16,17
Y	EP,A,0 442 011 (HEWLETT-PACKARD GMBH) 21 August 1991 see page 8, line 54 - page 11, line 40; figures 1-10 ---	16
X	EP,A,0 280 986 (SUMITOMO ELECTRIC INDUSTRIES LTD.) 7 September 1988	6
Y	see the whole document --- -/--	17

[X] Further documents are listed in the continuation of box C.   [X] Patent family members are listed in annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 July 1994	2 5. 08. 94

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hunt, B

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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